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# FACSIMILE TRANSMISSION

DATE: September 1, 2004

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	Office of Patent Publications U.S. Patent and Trademark Office	703-308-5083	

FROM: Charlene L. Yager

PHONE: (608) 283-4429

RE: U.S. Patent Application No. 09/741,272  
Charles Degenhardt, et al

NUMBER OF PAGES, INCLUDING COVER:		17
CLIENT MATTER NUMBER:	010785-9002	SENDER'S ACCOUNT NUMBER: 8853

**NOTES/COMMENTS:**

[illegible]

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Appl No. 09/741,272  
Amdt. dated September 1, 2001  
Reply to Office action of June 3, 2004

Appl. No. : 09/741,272  
Confirmation No. : 6508  
Applicant : Charles Degenhardt, et al.  
  
Filed : December 19, 2000  
Title : SUBSTITUTED PIPERIDINE  
AMIDES AND METHODS OF  
THEIR USE  
  
TC/A.U. : 1624  
Examiner : Thomas C. McKenzie  
  
Docket No. : 010785-9002-01

I, Sally Sorensen, hereby certify that this correspondence is being sent by facsimile to the Office of Patent Publications, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date of my signature.

Signature Sally Sorensen  
Date of Signature Sept. 1, 2004

AMENDMENT UNDER 37 C.F.R. § 1.312

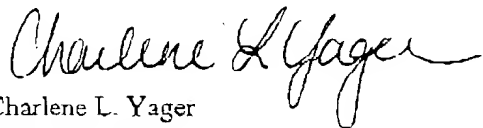
Office of Patent Publications  
Commissioner for Patents  
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Alexandria, VA 22313-1450

Dear Sir:

Applicants submit an additional copy of an Information Disclosure Statement submitted to the USPTO on April 26, 2001, for initialing by the Examiner. Applicants also include a copy of the return postcard that shows receipt by the USPTO mailroom on May 2, 2001.

Please contact the undersigned at 608-283-2249 should any questions remain.

Respectfully submitted,



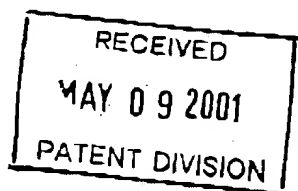
Charlene L. Yager  
Reg. No. 48,887

Docket No.: 010785-9002-01  
Michael Best & Friedrich LLP  
100 East Wisconsin Avenue  
Milwaukee, Wisconsin 53202-4108  
(414) 271-6560

ENCLOSURE 010785-9002-010418/21.1

Received: Information Disclosure Statement - 4 pages  
Copies of 8 copending applications  
PTO-1449 - 10 pages  
Cited references  
Return postcard  
Mailing under 37 CFR 1.8 dated 4/26/2001

Inventor: Degenhardt et al  
S/n: 09/740,272  
Filed: 12/19/2000  
Case: 8371  
CUB/keg



I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner For Patents, Washington, D.C. 20231 on April 26, 2000.

Catherine V. Brown	44,565
Name of Attorney/Agent	Registration No.
<i>Catherine V. Brown</i>	<i>[Signature]</i>
Signature of Attorney/Agent	

Case 8371

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Application of :  
**DEGENHARDT ET AL** :  
Serial No.: 09/741,272 : Group Art Unit. 1614  
Filed: 12/19/2000 : Examiner: Not assigned

For: 2-Substituted heterocyclic compounds

INFORMATION DISCLOSURE STATEMENT

Commissioner For Patents  
Washington, D.C. 20231

Dear Sir:

Pursuant to 37 C.F.R. §§ 1.56, 1.97 and 1.98, record is being made below in a Form PTO-1449 of documents which the Patent Office may wish to consider in connection with examination of the above-identified patent application. It is respectfully requested that the cited documents be carefully considered by the Examiner and made of record in this case. As provided in §1.97(g), no representation is made or intended that a thorough art search was made. As provided in 37 C.F.R. §1.97(h), this Information Disclosure Statement does not constitute an admission of any kind, and specifically is not an admission that the documents listed on attached form PTO-1449 are, or are considered to be, material to the patentability of the above-identified patent application, as defined in 37 C.F.R. §1.56(b).

1. ☐ 37 C.F.R. §1.97 (b)(1) - US. Direct (within 3-months of filing a regular application or converted provisional)

This information disclosure statement, submitted under 37 C.F.R. §1.97 (b)(1), is being filed within three months of the filing date of a national application. Therefore, no fee is believed to be due.

2. ☐ 37 C.F.R. §1.97 (b)(2) - Via PCT (within 3 mo. of Nat'l Stage Entry)

This information disclosure statement, submitted under 37 C.F.R. §1.97 (b)(2), is being filed within three months of the date of entry of the national stage as set forth in 37 C.F.R. §1.491 in an international application. Therefore, no fee is believed to be due.

3. ☒ 37 C.F.R. §1.97 (b)(3) - (>3 mo. after filing direct or nat'l stage entry, but before 1<sup>st</sup> O.A.)

This information disclosure statement is being submitted under 37 C.F.R. §1.97 (b)(3). Applicants have not received an Office Action on the merits in the present application. Therefore, no fee is believed to

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be due. However, in the event that this paper is crossing in the mail with a first Office Action on the merits, authorization is hereby given to charge the required fee pursuant to 37 C.F.R. §1.97(c) and 37 C.F.R. §1.17(p) to Deposit Account No. 16-2480 in the name of The Procter & Gamble Company. A duplicate of this letter is enclosed to facilitate charging of the fee, if necessary.

**THE FOLLOWING IS ADDITIONAL INFORMATION PERTAINING TO  
(2) OR (3) MARKED WITH AN (X) ABOVE.**

(a) ☐ The Notification of Acceptance of this Application Under 35 U.S.C. §371 indicates that both a copy of the International Search Report and copies of the references cited therein are present in the national stage file. In accordance with MPEP §1893.03(g), it is respectfully requested that the Examiner note the consideration of these references in the first Office Action via the PTO-892 form.

(b) ☐ The Notification of Acceptance of this Application Under 35 U.S.C. §371 indicates that a copy of the International Search Report is present in the national stage file. Copies of the references cited in that report are enclosed. It is respectfully requested that the Examiner note the consideration of these references in the first Office Action via the PTO-892 form.

(c) ☐ The Notification of Acceptance of this Application Under 35 U.S.C. §371 does not indicate that a copy of the International Search Report and copies of the references cited are present in the national stage file. Copies of the International Search Report and references are attached.

4. ☐ 37 C.F.R. §1.97(c) with fee payment - (use after 1<sup>st</sup> Office Action & before Final Office Action or Notice of Allowance)

This information disclosure statement is being submitted under 37 C.F.R. §1.97(c). Applicant(s) have not received a final action under 37 C.F.R. §1.113 or a notice of allowance under 37 C.F.R. §1.311 as of the date of this submission. Applicant(s) elect to pay the fee set forth in 37 C.F.R. §1.17(p). Please charge the fee set forth in 37 C.F.R. §1.17(p) to Deposit Account Number 16-2480 in the name of The Procter & Gamble Company. A duplicate copy of this letter is enclosed to facilitate the charging of the fee.

**ADDITIONAL ITEMS TO BE NOTED BY THE EXAMINER:**

☐ (1) Copies of the cited references were previously cited by or submitted to the USPTO in prior application Case No. \_\_\_\_, U.S. Patent Application Serial No. \_\_\_\_, filed \_\_\_\_. Applicants claim priority to said application under 35 U.S.C. §120. Accordingly, copies of those documents are not provided with this Statement, pursuant to 37 C.F.R. §1.98(d).

OR

☒ (2) Copies of the cited documents are enclosed.

OR

☐ (3) Copies of all said documents, except document No.'s \_\_\_\_, were submitted and considered in parent application U.S. Patent Application Serial No. \_\_\_\_, filed \_\_\_\_\_. Applicant(s) claim priority to said application under 35 U.S.C. §120. Accordingly, copies of document No.'s \_\_\_\_ are not provided with this Statement, pursuant to 37 C.F.R. §1.98(d). Copies of document No.'s \_\_\_\_ are enclosed. It is respectfully requested that the cited documents be carefully considered by the Examiner and made of record in this case.

☐ (4) Pursuant to 37 C.F.R. §1.98(e), a concise explanation of the relevance of each cited reference that is not in the English language is on the attached page, except where a full English language translation is provided.

☒ (5) Applicants also respectfully request the Examiner to consider and make of record the copending applications listed on the attached page, the copies of which are attached.

☐ Additional information is attached.

Respectfully submitted,

By Catherine U. Brown  
Catherine U. Brown  
Attorney for Applicant(s)  
Registration No. 44,565  
(513) 627-1637

April 6, 2001  
Miami Valley Labs

**COPENDING APPLICATIONS**

§ 1.98(a)(2) Content of information disclosure statement: Section 1.98(a)(2)(iii) requires submission of copies of U.S. patent applications that are being cited in IDS statements.

§ 1.98(d)(2) If a U.S. application was cited in an IDS prior to the effective date of the change to §1.98(a)(2) (now requiring a copy of the cited application) but a copy of the cited application was not supplied, as was permissible under the former rule, a copy of the cited application must be supplied if cited in any continuing application where the citation is made after the effective date of the changes to §§ 1.98(a) and (d).

<u>Atty. Docket No.</u>	<u>Serial Number</u>	<u>Inventor(s)</u>	<u>Filing Date</u>
8370	09/740,642	Degenhardt	12/19/2000
8372	09/741,588	Degenhardt	12/19/2000
8373	09/740,644	Degenhardt	12/19/2000
8374	09/740,387	Degenhardt	12/19/2000
8375	09/740,643	Degenhardt	12/19/2000
8376	09/740,388	Degenhardt	12/19/2000
8377	09/740,391	Degenhardt	12/19/2000
8378	09/740,279	Degenhardt	12/19/2000



LIST OF DOCUMENTS CITED BY APPLICANTS (Use several sheets if necessary)	ATTY. DOCKET NO. 8371	SERIAL NO. 09/741,272
	APPLICANT Degenhardt et al	
	FILING DATE 12/19/2000	GROUP 1646

## U. S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE IF APPROPRIATE
	1	4,923,871	3/0/1990	Inaba et al	C07D	401/04	
	2	4,985,558	1/15/1991	Suzuki et al	C07D	401/04	
	3	4,996,321	2/26/1991	Baldwin et al	C07D	211/70	
	4	5,114,919	5/19/1992	Baldwin et al	A61K	31/55	
	5	5,124,339	6/23/1992	KING	A01N	43/36	
	6	5,130,303	7/14/1992	Akiyama et al	A61K	31/44	
	7	5,160,727	11/3/1992	Klohe et al	A61K	49/00	
	8	5,173,486	12/22/1992	Monkovic et al	A61K	31/55	
	9	5,182,293	1/26/1993	Sunkara et al	A61K	31/44	
	10	5,190,946	3/2/1993	Hamu et al	A61K	31/495	
	11	5,190,957	3/2/1993	Sunkara et al	A61K	31/47	
	12	5,204,348	4/20/1993	Fukazawa et al	A61K	31/496	
	13	5,216,172	6/1/1993	TOYOTA ET AL	C07D	213/55	
	14	5,225,405	7/6/1993	Paramelle et al	A01N	66/02	
	15	5,238,936	8/24/1993	Regnier et al	C07D	401/04	
	16	5,272,159	12/21/1993	Baldwin et al	A61K	31/435	
	17	5,292,726	3/8/1994	Achton et al	A61K	31/675	
	18	5,292,757	3/8/1994	OHSUMI ET AL	C07D	211/00	
	19	5,302,727	4/12/1994	Eliason et al	C07D	339/08	
	20	5,336,685	8/9/1994	Prochaska et al	A61K	31/35	
	21	5,362,729	11/8/1994	Cozzi et al	C07D	401/06	
	22	5,371,081	12/6/1994	Houghton et al	A61K	31/535	
	23	5,389,844	2/14/1995	Peglion et al	A61K	31/44	
	24	5,409,600	4/25/1995	Howell et al	A61K	48/00	
	25	5,416,091	5/16/1995	KING	A61K	45/06	
	26	5,436,243	7/25/1995	Sachs et al	A61K	31/195	
	27	5,508,403	4/16/1996	Akiyama et al	C07F	9/6574	
	28	5,514,664	5/7/1996	Ulrich	A61K	31/70	
	29	5,516,775	5/14/1996	Zimmermann et al	A61K	31/505	
	30	5,521,184	5/28/1996	Zimmermann	C07D	239/92	
	31	5,523,304	6/4/1996	Sunkara	A61K	31/435	
	32	5,525,606	6/11/1996	Moschel et al	A61K	31/52	
	33	5,536,722	7/16/1996	Coe et al	C07D	251/70	
	34	5,541,232	7/30/1996	Howell et al	A61K	31/045	
	35	5,543,423	8/6/1996	Zelle et al	A61K	31/44	
	36	5,543,428	8/6/1996	Sawyer et al	A61K	31/35	
	37	5,550,149	8/27/1996	Powell et al	C07D	209/44	
	38	5,569,471	10/29/1996	Oguro	A61K	33/24	
	39	5,571,887	11/5/1996	Casey et al	C12Q	1/00	
	40	5,583,137	12/10/1996	Coe et al	C07D	473/16	
	41	5,610,185	3/11/1997	MacCoss et al	A61K	31/445	
	42	5,620,971	4/15/1997	ARMISTEAD ET AL	A61K	31/51	
	43	5,622,953	4/22/1997	Janeson et al	A61K	31/495	
	44	5,643,869	7/1/1997	Dreyfuss et al	A61K	38/00	
	45	5,654,304	8/5/1997	Pfister et al	A61K	31/50	
	46	5,663,179	9/2/1997	Dumaitre et al	C07D	401/12	
	47	5,670,508	9/23/1997	Wang et al	A61K	31/535	
	48	5,670,521	9/23/1997	Freedman et al	A01K	31/446	
	49	5,700,826	12/23/1997	Mjalli et al	A01K	31/415	
	50	5,723,459	3/3/1998	Armistead et al	A61K	31/64	
	51	5,726,184	3/10/1998	Zelle	C07D	211/00	
	52	5,733,911	3/31/1998	Ellon et al	A61K	31/495	
	53	5,744,485	4/20/1998	Zelle et al	C07D	211/32	
	54	5,756,475	5/26/1998	Inomata et al	A01N	43/04	

55	5,756,527	5/26/1998	Mjalli et al	A61K	31/415	
56	5,763,443	6/9/1998	Medlon et al	C07D	241/46	
57	5,775,939	7/7/1998	Kroin et al	A01N	43/60	
58	5,811,434	9/22/1998	Zello et al	C07D	211/60	
59	5,827,845	10/27/1998	Regenass et al	A61K	31/55	
60	5,840,721	11/24/1998	Mjalli et al	A61K	31/415	
61	5,852,018	12/22/1998	Bryans et al	A61K	31/495	
62	5,885,786	3/23/1999	Cabot	G01N	33/53	
63	5,935,954	8/10/1999	Armistead et al	C07D	211/60	

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRANSLATION YES NO	
64	CA	2,188,615	2/27/1997	Canada	A61K	31/36		X
65	EP	0428 104 A2	5/22/1991	EPO	A61K	31/44		X
66	EP	0428 107 A2	5/22/1991	EPO	A61K	31/37		X
67	EP	0529 395 A2	03/03/93	EPO	C07C	237/44		X
68	EP	0781 652 A1	7/2/1997	EPO	A61K	31/135		X
69	EP	0812 630 A1	12/17/1997	EPO	C07D	233/54		X
70	GB	2317 030 A	11/3/1998	Great Britain	G06F	17/50		X
71	JP	04356466	10/12/1992	Japan	C07D	215/20		X
72	WO	91/09846	7/11/1991	WIPO	C07D	211/90		X
73	WO	92/1232	7/23/1992	WIPO	C07D	219/06		X
74	WO	94/04513	3/3/1994	WIPO	C07D	241/00		X
75	WO	94/06771	3/31/1994	WIPO	C07D	221/18		X
76	WO	94/07858	4/14/1994	WIPO	C07D	211/60		X
77	WO	94/11382	5/26/1994	WIPO	C07H	17/00		X
78	WO	94/14809	7/7/1994	WIPO	C07D	471/04		X
79	WO	94/17040	8/4/1994	WIPO	C07D	211/16		X
80	WO	94/22846	10/13/1994	WIPO	C07D	277/64		X
81	WO	95/05824	3/2/1995	WIPO	A61K	31/44		X
82	WO	95/26337	10/5/1995	WIPO	C07D	211/60		X
83	WO	95/32975	12/7/1995	WIPO	C07D	498/22		X
84	WO	95/32976	12/7/1995	WIPO	C07D	498/22		X
85	WO	96/11677	4/25/1996	WIPO	A61K	31/135		X
86	WO	96/15101	5/23/1996	WIPO	C07C	237/02		X
87	WO	96/20179	7/4/1996	WIPO	C07D	241/02		X
88	WO	96/20180	7/4/1996	WIPO	C07D	241/02		X
89	WO	96/20190	7/4/1996	WIPO	C07D	401/12		X
90	WO	96/36630	11/21/1996	WIPO	C07D	401/12		X
91	WO	97/17069	5/15/1997	WIPO	A61K	31/38		X
92	WO	97/28166	8/7/1997	WIPO	C07D	495/04		X
93	WO	97/34897	9/23/1997	WIPO	C07D	487/04		X
94	WO	97/36868	10/9/1997	WIPO	C07D	211/60		X
95	WO	97/45120	12/4/1997	WIPO	A61K	31/495		X
96	WO	97/48689	12/24/1997	WIPO	C07D	295/088		X
97	WO	97/48708	12/24/1997	WIPO	C07D	515/22		X
98	WO	98/08822	3/5/1998	WIPO	C07D	239/04		X
99	WO	98/22112	5/28/1998	WIPO	A61K	31/495		X
100	WO	98/30653	7/16/1998	WIPO	C07D	305/14		X
101	WO	98/52923	5/22/1998	WIPO	C07D	219/06		X
102	WO	99/10340	3/4/1999	WIPO	C07D	401/12		X
103	WO	99/13871	3/23/1999	WIPO	A61K	31/00		X
104	WO	99/24401	5/20/1999	WIPO	C07D	211/46		X
105	WO	99/26921	6/3/1999	WIPO	C07D	207/16		X
106	WO	99/43323	9/2/1999	WIPO	A61K	31/495		X
107	WO	99/64001	12/16/1999	WIPO	A61K	31/47		X

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

1	Pajeva, I. et al, "A Comparative Molecular Field Analysis of Propafenone-type Modulators of Cancer Multidrug Resistance", <i>Quant. Struct. - Act. Relat.</i> , <b>17</b> , pg. 301-312, (1998)
2	Roe, M. et al, "Reversal of P-Glycoprotein Mediated Multidrug Resistance by Novel Anthranilamide Derivatives", <i>Bioorganic &amp; Medicinal Chemistry Letter</i> , <b>9</b> , pg. 595-600, (1999)
3	Chiba, P. et al, "Synthesis, Pharmacologic Activity, and Structure - Activity Relationships of a Series of Propafenone-related modulators of Multidrug Resistance", <i>J. Med. Chemistry</i> , <b>38</b> , pg. 2789-2793, (1995)
4	Ecker, G. et al, "Structure - Activity Relationship Studies on Benzofuran Analogs of Propafenone-type Modulators of Tumor Cell Multidrug Resistance", <i>Journal of Medicinal Chemistry</i> , <b>39</b> , pg. 4767-4774 (1996)
5	Chiba, P. et al, "Structural Requirements for Activity of Propafenone-type Modulators in P-Glycoprotein-Mediated Multidrug Resistance", <i>Molecular Pharmacology</i> , <b>49</b> , pg. 1122-1130, (1996)
6	Chiba, P. et al, "Synthesis and Pharmacological activity of the stereoisomers of GP-88, a Propafenone-type modulator of Multidrug resistance", <i>Bioorganic &amp; Medicinal Chemistry Letter</i> , <b>8</b> , pg. 829-832, (1998)
7	Chiba, P. et al, "Studies on Propafenone-type Modulators of Multidrug Resistance III: Variations on the Nitrogen", <i>Quant. Struct.-Act. Relat.</i> , <b>16</b> , pg. 361-366 (1997)
8	Chiba, P. et al "Studies on Propafenone-type Modulators of Multidrug-resistance IV: Synthesis and Pharmacological Activity of 5-Hydroxy and 5-Benzyloxy", <i>Arch. Pharm. Pharm. Med. Chem.</i> , <b>330</b> , pg. 343-347 (1997)
9	Oberlies, N. et al, "Structure - Activity Relationships of Diverse Annonaceous Acetogenins against Multidrug Resistant Human mammary Adenocarcinoma (MCF-7/Adr) Cells", <i>Journal of Medicinal Chemistry</i> , <b>40</b> , pg. 2102-2106, (1997)
10	Conseil, G. et al, "Flavonoids: A class of modulators with bifunctional interactions at vicinal ATP- and steroid-binding sites on mouse P-glycoprotein", <i>Biochemistry</i> , <b>35</b> , pg. 9831-9836, (1996)
11	Ferte, J. et al, "Flavonoid-Related Modulators of Multidrug Resistance: Synthesis, Pharmacological Activity, and Structure - Activity Relationships", <i>J. Med. Chemistry</i> , <b>42</b> , pg. 478-489 (1999)
12	Merritt, J. et al, "The bisindolylmaleimide protein kinase C inhibitor, Ro 32-2241, reverses multidrug resistance in KB tumor cells", <i>Cancer Chemother Pharmacol.</i> , <b>43</b> , pg. 371-378, (1999)
13	Payen, L. et al, "Reversal of MRP-Mediated Multidrug Resistance in Human lung Cancer Cells by the Antiprogesterin Drug RU486" <i>Biochemical and Biophysical Research Communications</i> , <b>258</b> , pg. 513-518, (1999)
14	Fukushima, T. et al, "Effect of PSC 833 on the cytotoxicity of idarubicin and idarubicinol in the multidrug-resistant K562 cells", <i>Leukemia Research</i> , <b>23</b> , pg. 37-42, (1999)
15	Berger, D. et al, "Novel Multidrug Resistance Reversal Agents", <i>Journal Medicinal Chemistry</i> , <b>42</b> , pg. 2145-2161, (1999)
16	Roe, M. et al, "Reversal of P-Glycoprotein Mediated Multidrug Resistance by Novel anthranilamide Derivatives", <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , <b>9</b> , pg. 595-600, (1999)
17	Chiba, P. et al, "Substituted 4-Acylpyrazoles and 4-Acylpyrazolones: Synthesis and Multidrug Resistance-Modulating Activity", <i>J. Med. Chem.</i> , <b>41</b> , pg. 4001-4011, (1998)
18	Sawantshi, H. et al, "Novel Inhibitors for Multidrug Resistance: 1,3,5-Triazacycloheptanes", <i>J. Med. Chem.</i> , <b>38</b> , pg. 5066-5070, (1995)
19	Dhainaut, A. et al, "New Purine and Purine Analogs as Modulators of Multidrug Resistance", <i>J. Med. Chem.</i> , <b>39</b> , pg. 4099-4108, (1996)
20	Suzuki, T. et al, "Structure - Activity Relationship of Newly Synthesized Quinoline derivatives for Reversal of Multidrug Resistance in Cancer", <i>Journal of Medicinal Chemistry</i> , <b>40</b> , pg. 2047-2052, (1997)
21	Dinh, T. et al, "Design, Synthesis, and Evaluation of the Multidrug Resistance-Reversing activity of D-Glucose Mimetics of Hapalosin", <i>Journal of Medicinal Chemistry</i> , <b>41</b> , pg. 981-987 (1998)
22	Dinh, T. et al, "Synthesis, Conformational Analysis, and Evaluation of the Multidrug Resistance-Reversing Activity of the Triamide and Proline Analogs of Hapalosin", <i>J. of Organic Chemistry</i> , <b>62</b> , pg. 6773-6783, (1997)
23	Dhainaut, A. et al, "New Triazine derivatives as Potent Modulators of Multidrug Resistance", <i>Journal of Medicinal Chemistry</i> , <b>35</b> , pg. 2481-2496, (1992)
24	Thimmiah, K. et al, "Synthesis and Chemical Characterization of N-Substituted Phenoxazines Directed toward Reversing Vinca Alkaloid Resistance in Multidrug-Resistance Cancer Cells", <i>Journal of Medicinal Chemistry</i> , <b>35</b> , pg. 3359-3364, (1992)
25	Bois, F. et al, "Halogenated Chalcones with High-Affinity Binding to P-Glycoprotein: Potential Modulators of Multidrug Resistance", <i>Journal of Medicinal Chemistry</i> , <b>41</b> , pg. 4161-4164 (1998)
26	Emmer, G. et al, "Derivatives of a Novel Cyclopeptide. 2. Synthesis, Activity against Multidrug Resistance in CHO and KB cells <i>In Vitro</i> , and Structure-Activity Relationships", <i>Journal of Medicinal Chemistry</i> , <b>37</b> , pg. 1916-1929 (1994)
27	Andrus, M. et al, "Total Synthesis of Stipamide and designed Polyones as new Agents for the Reversal of Multidrug Resistance", <i>J. American Chemical Society</i> , <b>119</b> , pg. 12159-12169 (1997)

## OTHER DOCUMENTS Continued

28	Tasaka, S. et al, "Synthesis of 2-Phenylimidazo [2,1-b]benzothiazole Derivatives as Modulators of Multidrug Resistance for Tumor Cells", <i>J. Heterocyclic Chem.</i> , <b>31</b> , pg. 1763-1767 (1997)
29	Morihira, K. et al, "Synthesis and Evaluation of Artificial Taxoids with Antitumor and Multi-Drug resistance Reversing Activities", <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , <b>8</b> , pg. 2977-2982 (1998)
30	Morihira, K. et al, "Synthesis of C-Ring Aromatic Taxoids and Evaluation of Their Multi-Drug Resistance reversing activity", <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , <b>8</b> , pg. 2973-2976, (1998)
31	Kobayashi, J. et al, "Modulation of the Multidrug Resistance by a Taxuspine C and Other Taxoids from <i>Japaneos Yew</i> ", <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , <b>8</b> , pg. 1555-1558, (1998)
32	Kobayashi, J. et al, "Effects of Taxoids from <i>taxus cuspidata</i> on microtubule depolymerization and vincristine accumulation in MDR cells", <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , <b>7</b> , pg. 393-398 (1997)
33	Hosoyama, H. et al, "Modulation of Multidrug Resistance in Tumor Cells by Taxinine derivatives", <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , <b>9</b> , pg. 389-394, (1999)
34	Kami, T. et al, "Reversal of Multidrug resistance (MDR) by aspidofractinine-type indole alkaloids", <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , <b>8</b> , pg. 2769-2772, (1998)
35	Tanabe, H. et al, "Newly Synthesized Dihydropyridine Derivatives as Modulators of P-Glycoprotein-mediated Multidrug Resistance", <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , <b>6</b> , pg. 2219-2227 (1998)
36	Sawanishi, H. et al, "Structure-activity Relationships of Diamines, Dicarboxamides, and Disulfonamides on Vinblastine accumulation in P388/ADR Cells", <i>Chem. Pharm. Bull.</i> , <b>7</b> , pg. 1459-1462, (1994)
37	Hooijberg, J. et al, "Modulation by (iso)flavonoids of the ATPase activity of the multidrug resistance protein", <i>FEBS Letters</i> , <b>413</b> , pg. 344-348, (1997)
38	Sarkadi, B. et al, "Interaction of bioactive hydrophobic peptides with the human multidrug transporter", <i>The FASEB Journal</i> , <b>8</b> , pg. 766-770, (1994)
39	Pereira, F. et al, "Reversal of Multidrug Resistance by Verapamil analogues", <i>Biochemical Pharmacology</i> , vol. <b>50</b> , no. <b>1</b> , pg. 451-457, (1995)
40	Pommerenke, E. et al, "Activity of various amphiphilic agents in reversing multidrug resistance of L1210 cells", <i>Cancer Letters</i> , <b>55</b> , pg. 17-23, (1990)
41	Kiue, A. et al, "Activities of Newly Synthesized Dihydropyridines in Overcoming of Vincristine Resistance, Calcium Antagonism, and Inhibition of Photoaffinity labeling of P-Glycoprotein in Rodents", <i>Cancer Research</i> , <b>50</b> , pg. 310-317, (1990)
42	Ford, J. et al, "Structural Features Determining Activity of Phenothiazines and Related Drugs for Inhibition of Cell Growth and Reversal of Multidrug resistance", <i>Molecular Pharmacology</i> , <b>35</b> , pg. 105-115
43	Nogae, I. et al, "Analysis of structural features of dihydropyridine analogs needed to reverse multidrug resistance and to inhibit photoaffinity labeling of P-glycoprotein", <i>Biochemical Pharmacology</i> , <b>38</b> , pg. 519-527, (1989)
44	Pedro, H. et al, "Essential features of the P-glycoprotein pharmacophore as defined by a series of reserpine analogs that modulate multidrug resistance", <i>Proc. Natl. Acad. Sci.</i> , <b>86</b> , pg. 5128-5132 (1989)
45	Kirk, J. et al, "Reversal of P-glycoprotein-mediated multidrug resistance by pure anti-oestrogens and novel tamoxifen derivatives", <i>Biochemical Pharmacology</i> , <b>48</b> , pg. 277-285, (1994)
46	Gokeler, V. et al, "The specific bisindolymaleimide PKC-Inhibitor GF 109203x efficiently modulates MRP-Associated Multiple drug resistance", <i>Biochemical and Biophysical research communications</i> , <b>206</b> , pg. 119-126, (1995)
47	Ford, J. et al, "Cellular and Biochemical Characterization of Thioxanthines for Reversal of Multidrug resistance in Human and Murine Cell Lines", <i>Cancer Research</i> , <b>50</b> , pg. 1748-1756, (1990)
48	Kadam, S. et al, "Reversal of Multidrug Resistance by Two Novel Indole Derivatives", <i>Cancer Research</i> , <b>52</b> , pg. 4735-4740, (1992)
49	Dollinger, M. et al, "Structural Requirements of Simple Organic Cations for Recognition by Multidrug-resistant cells", <i>Cancer research</i> , <b>52</b> , pg. 6385-6389, (1992)
50	Horton, J. et al, "Pharmacological Characterization of N-Substituted Phenoxazines Directed toward reversing vinca alkaloid resistance in multidrug-resistant cancer cells", <i>Molecular Pharmacology</i> , <b>44</b> , pg. 552-559, (1993)
51	Smith, C. et al, "Wolwidolinone Analogues that reverse P-Glycoprotein-Mediated Multiple drug Resistance", <i>Molecular Pharmacology</i> , <b>47</b> , pg. 241-247, (1995)
52	Zhang, L. et al, "Characterization of Prenylcysteines that interact with P-glycoprotein and Inhibit Drug transport in tumor cells", <i>The Journal of Biological Chemistry</i> , <b>270</b> , pg. 22859-22865 (1995)
53	Hofmann, J. et al, "Mechanism of action of dexniguldipine-HCl (B8509-035), a new potent modulator of multidrug resistance", <i>Biochemical Pharmacology</i> , <b>49</b> , pg. 603-609 (1995)
54	Wakusawa, S. et al, "Overcoming of Vinblastine Resistance by Isoquinolinesulfonamide compounds in Adriamycin-Resistant Leukemia Cells", <i>Molecular Pharmacology</i> , <b>41</b> , 1034-1038 (1992)
55	Eliason, J. et al, "Novel Dithiane analogues of tiapamil with high activity to overcome multidrug resistance in vitro", <i>Biochemical Pharmacology</i> , <b>50</b> , pg. 187-196, (1995)
56	Bhat, U. et al, "A structure-Function Relationship among Reserpine and Yohimbine Analogues in Their Ability to Increase expression of <i>mdr1</i> and P-Glycoprotein in a human colon carcinoma cell line", <i>Molecular Pharmacology</i> , <b>48</b> , pg. 682-689 (1995)

## OTHER DOCUMENTS Continued

57	Borrel, M. et al, "The effect of crown ethers, tetraalkylammonium salts, and polyoxyethylene amphiphiles on pirarubicin incorporation in K562 resistant cells" <i>Biochemical Pharmacology</i> , 50, pp. 2069-2076 (1995)
58	Toffoli, G. et al, "Structure-Activity relationship of verapamil analogs and reversal of multidrug resistance" <i>Biochemical Pharmacology</i> , 50, pp. 1245-1255, (1995)
59	Christensen, J. et al, "Reversal of multidrug resistance in vivo by dietary administration of the phytochemical Indole-3-Carbinol", <i>Cancer Research</i> , 56, pp. 574-581, (1996)
60	Barnes, K. et al, "Steroid Transport, accumulation, and antagonism of P-Glycoprotein in Multidrug resistant cells" <i>Biochemistry</i> , 35, pp. 4820-4827, (1996)
61	Frappier, F. et al, "Bisbenzylisoquinolines as Modulators of Chloroquine Resistance in Plasmodium falciparum and multidrug resistance in Tumor cells" <i>Antimicrobial Agents and Chemotherapy</i> , June, pp. 1476-1481, (1996)
62	Nakamura, S. et al, "Inhibition of P-Glycoprotein-Dependent Multidrug Resistance by an Isoquinolinesulfonamide Compound H-87 in Rat Ascites Hepatoma AH66 Cells" <i>Biol. Pharm. Bull.</i> , 19, pp. 886-889, (1996)
63	Iidaka, H. et al, "Isoquinolinesulfonamides, Novel and Potent Inhibitors of Cyclic Nucleotide dependent Protein Kinase and Protein Kinase C", <i>Biochemistry</i> , 23, pp. 5036-5041, (1984)
64	Chou, T. et al, "Reversal of anticancer multidrug resistance by the ardeemins" <i>Proc. Natl. Acad. Sci.</i> , 95, pp. 8369-8374, (1998)
65	Vanhoefor, U. et al, "PAK-104P, a Pyridine analogue, Reverses Paclitaxel and Doxorubicin Resistance in cell Lines and Nude Mice Bearing Xenografts that overexpress the multidrug resistance protein" <i>Clinical Cancer Research</i> , 2, pp. 369-377 (1996)
66	Chaudhary, P. et al, "Induction of Multidrug Resistance in Human Cells by Transient Exposure to different Chemotherapeutic Drugs" <i>Journal of the National Cancer Institute</i> , 85, pp. 632-639 (1993)
67	Sharon, F. et al, "Linear and cyclic peptides as substrates and modulators of P-glycoprotein, peptide binding and effects on drug transport and accumulation" <i>Biochem. Journal</i> , 333, pp. 621-630 (1998)
68	Decrayaud, S. et al, "Effect of the Mdr1a P-Glycoprotein Gene disruption on the tissue distribution of SDZ PSC 833, a multidrug Resistance-Reversing Agent, in Mice." <i>The Journal of Pharmacology and Experimental Therapeutics</i> , 285, pp. 438-443 (1998)
69	Watarabe, T. et al, "Effect of SDZ PSC 833 ([3'-keto-Bmt]-[Val]-cyclosporin) on serum protein binding and distribution to blood cells of doxorubicin, vincristine and etoposide in vitro" <i>Anti-Cancer Drugs</i> , 8, pp. 400-404 (1997)
70	Germann, U. et al, "Cellular and biochemical characterization of VX-710 as a chemosensitizer: reversal of P-glycoprotein-mediated multidrug resistance in vitro" <i>Anti-cancer drugs</i> , 8, pp. 125-140 (1997)
71	Shah, A. et al, "6,12-Dihydro-1-benzopyrano [3,4 b][1,4] benzothiazin-6-ones: Synthesis and mdr Reversal in Tumor Cells" <i>Anticancer Research</i> , 18, pp. 3001-3004 (1998)
72	Pajeva, I. et al, "Molecular Modeling of Phospholazines and Related Drugs as multidrug resistance modifiers: A Comparative molecular field analysis study" <i>Journal of Medicinal Chemistry</i> , 41, pp. 1815-1826 (1998)
73	Pajeva, I. et al, "QSAR and Molecular Modelling of Catamphiphilic Drugs Able to Modulate Multidrug resistance in Tumors" <i>Quant. Struct. - Act. Relat.</i> , 16, pp. 1-10 (1997)
74	Atadja, P. et al, "PSC-833, a frontier in modulation of P-glycoprotein mediated multidrug resistance", <i>Cancer and Metastasis Reviews</i> , 17, pp. 163-168, (1998)
75	Fields, A. et al, "PSC833: initial clinical results in refractory ovarian cancer patients" <i>Current Opinion in Oncology</i> , 10, pp. S21 (1998)
76	Demeule, M. et al, "Molecular Interactions of Cyclosporin A with P-glycoprotein" <i>The Journal of Biological Chemistry</i> , 272, pp. 6647-6652 (1997)
77	Puurtier-Manzanedo, A. et al, "SDZ PSC 833 and SDZ 280-446 are the most active of various resistance-modifying agents in restoring rhodamine-123 retention within multidrug resistant P388 cells" <i>Anti-Cancer Drugs</i> , 3, pp. 419-425 (1992)
78	Jachaz, B. et al, "SDZ 280-125, a cyclopeptolide endowed with an in vitro cyclosporin A-like profile of activity for the reversion to the P-glycoprotein-mediated multidrug resistance of tumor cells", <i>Anti-Cancer Drugs</i> , 5, pp. 313-320 (1994)
79	Twentyman, Peter R., "Cyclosporins as drug resistance modifiers", <i>Biochemical Pharmacology</i> , 43, pp. 109-117, (1992)
80	Germann, U. et al, "Chemosensitization and drug accumulation effects of VX-710, verapamil, cyclosporin A, MS-209 and CF120018 in multidrug resistant HL60/ADR cells expressing the multidrug resistance-associated protein MRP" <i>Anti-Cancer Drugs</i> , 8, pp. 141-155 (1997)
81	Dantzig, A. et al, "Reversal of P-Glycoprotein-mediated Multidrug Resistance by a Potent Cyclopropylidibenzosuberone Modulator, LY335979" <i>Cancer Research</i> , 56, pp. 4171-4179, (1996)
82	Starling, J. et al, "Pharmacological Characterization of LY335979: A Potent Cyclopropylidibenzosuberone Modulator of P-Glycoprotein" <i>Advan. Enzyme Regul.</i> , 37, pp. 335-347, (1997)
83	Pfister, J. et al, "Mathanodibenzosuberolpiperazines as Potent Multidrug Resistance Reversal Agents" <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , 5, pp. 2473-2476 (1995)

## OTHER DOCUMENTS Continued

84	Klopman, G. et al, "Structure-Activity study and Design of Multidrug-resistant Reversal Compounds by a Computer Automated Structure Evaluation Methodology" <i>Cancer Research</i> , 52, pg. 4121-4129 (1992)
85	Klopman, G. et al, "Quantitative Structure-Activity Relationship of Multidrug-Resistance Reversal Agents" <i>Molecular Pharmacology</i> , 52, pg. 323-334 (1997)
86	Legrand, O. et al "NEOPLASIA: Simultaneous Activity of MRP1 and Pgp is Correlated with in vitro resistance to Daunorubicin and with In vivo resistance in Adult Acute Myeloid Leukemia" <i>Blood</i> , 94, pg. 1046-1056 (1999)
87	Lelith, C. et al, "NEOPLASIA: Frequency and Clinical Significance of the Expression of the Multidrug resistance proteins MDR1/P-Glycoprotein, MRP1, and LRP in Acute Myeloid Leukemia. A Southwest Oncology Group Study." <i>Blood</i> , 81, pg. 1086-1099 (1993)
88	Mealey, K. et al, "Immunosuppressant inhibition of P-glycoprotein function is independent of drug-induced suppression of Peptide-prolyl isomerase and calcineurin activity" <i>Cancer Chemother Pharmacol</i> , 44, pg. 152-158, (1999)
89	Dey, S. et al, "A single amino acid residue contributes to distinct mechanisms of inhibition of the human multidrug transporter by stereoisomers of the dopamine receptor antagonist flupentixol" <i>Biochemistry</i> , 38, pg. 6630-6639 (1999)
90	Woo, T. et al "The transmembrane domains of the human multidrug resistance P-glycoprotein are sufficient to mediate drug binding and trafficking to the cell surface." <i>The Journal of Biological Chemistry</i> , 274, pg. 24753-24765, (1999)
91	Tunggal, J. et al, "Influence of cell concentration in limiting the therapeutic benefit of P-glycoprotein reversal agents" <i>Int. J. Cancer</i> , 81, pg. 741-747 (1999)
92	Zheleznova, E. et al, "A structure-based mechanism for drug binding by multidrug transporters, pg. 39-43, (year)
93	Di Piero, A. et al, "P-glycoprotein-mediated resistance to chemotherapy in cancer cells: using recombinant cytosolic domains to establish structure-function relationships" <i>Brazilian J. Med. Biol. Research</i> , 32, pg. 925-939 (1999)
94	Gray, M. et al, "Effect on cell kill of addition of multidrug resistance modifiers cyclosporin A and PSC 833 to cytotoxic agents in chronic lymphocytic leukaemia" <i>Leukemia Research</i> , 23, pg. 29-35 (1999)
95	Dey, S. et al, "Evidence for two nonidentical drug-interaction sites in the human P-glycoprotein", <i>Proc. Natl. Acad. Sci.</i> , 94, pg. 10594-10599 (1997)
96	Seeling, A. "A general pattern for substrate recognition by P-Glycoprotein" <i>Eur. Journal Biochem.</i> , 251, pg. 252-261 (1998)
97	Tmej, C. et al, "A Combined Hansch-Free Wilson Approach as Predictive Tool in QSAR Studies on Propafenone-Type Modulators of Multidrug Resistance" <i>Arch. Pharm. Pharm. Mod. Chem.</i> , 331, pg. 233-240 (1990)
98	Pearce, H. et al "Structural characteristics of compounds that modulate P-Glycoprotein-associated multidrug resistance" <i>Advances in Enzyme Regulations</i> , 30, pg. 357-373, (1990)
99	Safa, A. "Photoaffinity Labels for Characterizing Drug Interaction Sites of P-Glycoprotein" <i>Methods in Enzymology</i> , 292, pg. 289-307 (1998)
100	Zhu, B. T. "A Novel Hypothesis for the Mechanism of Action of P-Glycoprotein as a Multidrug Transporter" <i>Molecular Carcinogenesis</i> , 25, pg. 1-13 (1999)
101	Robert, J. "Proposals for Concomitant Use of several modulators of Multidrug Resistance in Clinics" <i>Anticancer Research</i> , 14, pg. 2371-2374 (1994)
102	Herrnway, C et al "Immunosuppressant Target Protein FKBP12 Is Required for P-Glycoprotein Function in Yeast", <i>The Journal of Biological Chemistry</i> , 271, pg. 18527-18531 (1996)
103	Tiberghien, F. et al "Ranking of P-glycoprotein substrates and inhibitors by a calcein-AM fluorimetry screening assay" <i>Anti-Cancer Drugs</i> , 7, pg. 568-578 (1996)
104	Scala, E. et al "P-Glycoprotein Substrates and Antagonists Cluster into Two Distinct Groups" <i>Molecular Pharmacology</i> , 51, pg. 1024-1033 (1997)
105	Carrico, M. et al "Competitive and non-competitive inhibition of the multidrug-resistance-associated P-glycoprotein ATPase: further experimental evidence for a multisite model" <i>Euro J. Biochem.</i> , 244, pg. 664-673 (1997)
106	Litman, T. et al "Structure-activity relationships of P-glycoprotein interacting drugs: kinetic characterization of their effects on ATPase activity" <i>Biochimica et Biophysica Acta</i> , 1361, pg. 159-168, (1997)
107	Wiese, M. et al "Molecular modeling study of the multidrug resistance modifiers cis- and trans-flupentixol." <i>Pharmazie</i> , 52, pg. 679-685 (1997)
108	Norman, B. "Inhibitors of MRP1-mediated multidrug resistance" <i>Drugs of the Future</i> , 23, pg. 1001-1013 (1998)
109	Robert, J. "Multidrug resistance reversal agents" <i>Drugs of the Future</i> , 22, pg. 149-158 (1997)
110	Ambudkar, S. et al "Biochemical, Cellular, and Pharmacological Aspects of the multidrug transporter" <i>Annu. Rev. Pharmacol. Toxicol.</i> , 39, pg. 361-398, (1999)
111	Sharom, F. et al "Spectroscopic and biophysical approaches for studying the structure and function of the P-glycoprotein multidrug transporter" <i>Biochem. Cell Biol.</i> , 76, pg. 695-708 (1998)

OTHER DOCUMENTS *Continued*

112	Borst, P., "Multidrug resistance: A solvable problem?" <i>Annals of Oncology</i> , 10, pg. S162-S164, (1999)
113	Sonneveld, P., "Drug resistance in Multiple Myeloma" <i>Pathologie et Biologie</i> , 47, pg. 182-187, (1999)
114	Luvi, F., "Valspodar: Current status and Perspectives" <i>Expert Opin. Invest. Drugs</i> , 8, pg. 807-835 (1999)
115	Opina, I. et al "Designing taxanes to treat multidrug-resistant tumors" <i>Modern Drug Discovery</i> , pg. 45-52 (1999)
116	Ueda, K. et al "Recent progress in P-Glycoprotein research" <i>Anti-Cancer Drug Design</i> , 14, pg. 115-121 (1999)
117	Ford, J. et al "Pharmacologic circumvention of multidrug resistance" <i>Cytotechnology</i> , 12, pg. 171-212, (1993)
118	Sonneveld, P. et al "Inhibitors of multidrug resistance" <i>Current Opinion in Oncology</i> , 9, pg. 643-648, (1997)
119	Hegewisch-Becker, S., "MDR1 Reversal: Criteria for clinical trials designed to overcome the multidrug resistance phenotype" <i>Leukemia</i> , 10, pg. S32-S38, (1996)
120	Volm, M., "Multidrug Resistance and its Reversal" <i>Anticancer Research</i> , 18, pg. 2905-2918 (1998)
121	Kavallaris, M., "The role of multidrug resistance-associated protein (MRP) expression in multidrug resistance" <i>Anti-Cancer Drugs</i> , 9, pg. 17-26, (1997)
122	Patel, N. et al "Multidrug resistance in cancer chemotherapy" <i>Investigational New Drugs</i> , 12, pg. 1-13, (1994)
123	Hegewisch-Becker, S. et al "The MDR phenotype in hematologic malignancies: prognostic relevance and future perspectives" <i>Ann Hematol</i> , 72, pg. 105-117 (1996)
124	Prost, S., "Mechanisms of Resistance to Topoisomerase Poisons" <i>Gen. Pharmac.</i> , 26, pg. 1773-1784 (1995)
125	Aszalos, A., "Modulation of Multidrug Resistance in Cancer by Immunosuppressive Agents" <i>Pathology Oncology Research</i> , 1, pg. 64-70, (1995)
126	Tsuruo, T. et al "Multidrug Resistance" <i>Anti-cancer Drugs</i> , 6, pg. 213-218 (1995)
127	Caponigro, F. et al "Protein kinase C: a worthwhile target for anticancer drugs?" <i>Anti-cancer Drugs</i> , 9, pg. 26-33 (1997)
128	Simon, S. et al "Cell biological mechanisms of multidrug resistance in tumors" <i>Proc. Natl. Acad. Sci.</i> , 91, pg. 3497-3504, (1994)
129	Inor, F., "Cyclosporins and Related Fungal Products in the Reversal of P-Glycoprotein-mediated Multidrug resistance" <i>Multidrug Resistance in Cancer Cells</i> , Chapter 26, pg. 385-412, (1996)
130	Lum, B. et al "Molecular Targets in Oncology. Implications of the Multidrug Resistance Gene" <i>Pharmacotherapy</i> , 13, pg. 88-109, (1993)
131	Sinha, B., "Topoisomerase Inhibitors" <i>Drugs</i> , 40, pg. 11-19, (1995)
132	Naito, M. et al "New Multidrug-resistance-reversing drugs, MS 209 and SDZ PSC 833" <i>Cancer Chemother Pharmacol</i> , 40, pg. S20-S24, (1997)
133	Ramu, A. et al "Reversal of multidrug resistance by phenothiazines and structurally related compounds" <i>Cancer Chemother Pharmacol</i> , 30, pg. 165-173 (1992)
134	Ramu, A. et al "Reversal of multidrug resistance by bis(phenylalkyl)amines and structurally related compounds" <i>Cancer Chemother Pharmacol</i> , 34, pg. 423-430, (1994)
135	Demeule, M. et al "Inhibition of P-glycoprotein by cyclosporin A analogues and metabolites" <i>Biochem. Cell Biol.</i> , 77, pg. 47-58, (1999)
136	Norman, B. et al "Reversal of Resistance in multidrug resistance protein (MRP1)-overexpressing cells by LY328146" <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , 9, pg. 3381-3386, (1999)
137	He, H. et al "Fumitremorgin C Analogs that reverse mitoxantrone resistance in human colon carcinoma cells" <i>Med. Chem. Res.</i> , 9, pg. 424-437 (1999)
138	Sparreboom, A. et al "Clinical pharmacokinetics of doxorubicin in combination with GF120918, a potent inhibitor of MDR1 P-glycoprotein" <i>Anti-Cancer Drugs</i> , 10, pg. 719-726, (1999)
139	Hooijberg, J. et al "Potent interaction of flavopindol with MRP1" <i>British Journal of Cancer</i> , 8, pg. 269-276 (1999)
140	Drewe, J. et al "HIV Protease Inhibitor Ritonavir: A More Potent Inhibitor of P-Glycoprotein than the Cyclosporine Analog SDZ PSC 833" <i>Biochemical Pharmacology</i> , 57, pg. 1147-1152, (1999)
141	Mendez-Vidal, C. et al "Reversal of P-glycoprotein-mediated multidrug resistance in vitro by AV200, a new ardeemin derivative" <i>Cancer Letters</i> , 132, pg. 45-50, (1998)
142	Dantzig, A. et al "Selectivity of the Multidrug Resistance Modulator, LY335979, for P-Glycoprotein and Effect on Cytochrome P-450 Activities" <i>The Journal of Pharmacology and Experimental Therapeutics</i> , 290, pg. 854-862, (1999)
143	Ecker, G. et al "The Importance of a Nitrogen Atom in Modulators of Multidrug resistance" <i>Molecular Pharmacology</i> , 56, pg. 791-796 (1999)
144	Lehne, G. et al "Growth inhibition, cytokinesis failure and apoptosis of multidrug-resistant leukemia cells after treatment with P-glycoprotein inhibitory agents" <i>Leukemia</i> , 13, pg. 768-778 (1999)
145	Regina, A. et al "Dexamethasone Regulation of P-Glycoprotein Activity in an Immortalized Rat Brain Endothelial Cell Line, GPNT" <i>Journal of Neurochemistry</i> , 73, pg. 1954-1963, (1999)



## OTHER DOCUMENTS Continued

146	Kim, S. et al "Sesquiterpene Esters from <i>Celastrus orbiculatus</i> and their structure-activity relationship on the modulation of multidrug resistance" <i>J. Nat. Prod.</i> , <b>62</b> , pp. 697-700, (1999)
147	Greenberger, L. et al "A-(3,4-Dimethoxyphenyl)-3,4-dihydro-6,7-dimethoxy-a-[(4-methylphenyl)thio]-2(1H)-iso-quinolineheptanenitrile (CL329,753): A Novel Chemosensitizing Agent for P-Glycoprotein-Mediated Resistance with Improved Biological Properties Compared with Verapamil and Cyclosporine A" <i>Oncology Research</i> , <b>8</b> , pp. 207-218, (1996)
148	Nakanishi, O. et al "Potentiation of the Antitumor Activity by a Novel Quinoline Compound, MS-209, in Multidrug-Resistant Solid Tumor Cell Lines", <i>Oncology Research</i> , <b>9</b> , pp. 61-69 (1997)
149	Kraus-Berthier, L. et al. "InVivo reversal of multidrug resistance by two new dihydropyridine derivatives, S16317 and S16324." <i>Acta Oncologica</i> , <b>33</b> , pp. 631-637, (1994)
150	Sato, W. et al "Reversal of multidrug resistance by a novel quinoline derivative, MS-209", <i>Cancer Chemother Pharmacol</i> , <b>35</b> , pp. 271-277 (1995)
151	O'Connell, C. et al "Synthesis and Evaluation of Hapalosin and analogs as MDR-Reversing agents" <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , <b>9</b> , pp. 1541-1546 (1999)
152	Hait, W. et al "Rational design and pre-clinical pharmacology of drugs for reversing multidrug resistance" <i>Biochemical Pharmacology</i> , <b>43</b> , pp. 103-107, (1992)
153	Liu, Z. et al "BIBW22 BS, Potent Multidrug resistance-Reversing Agent, Binds directly to P-Glycoprotein and Accumulates in Drug-Resistant Cells", <i>Molecular Pharmacology</i> , <b>50</b> , pp. 482-492, (1996)
154	Kwon, Y. et al "Inhibitors of P-Glycoprotein-mediated Daunomycin Transport in Rat Liver Canalicular Membrane Vesicles" <i>Journal of Pharmaceutical Sciences</i> , <b>85</b> , pp. 935-939, (1996)
155	Twentymen, P. et al "Effects of cyclosporin A and a non immunosuppressive analogue, O-acetyl cyclosporin A, upon a growth of parent and multidrug resistant human lung cancer cells <i>in vitro</i> ", <i>Br. J. Cancer</i> , <b>65</b> , pp. 335-340 (1992)
156	Okuno, T. et al "Chemical Study on Hapalosin, a Cyclic Depsipeptide Possessing Multidrug Resistance Reversing activities: Synthesis, Structure and Biological Activity" <i>Tetrahedron</i> , <b>52</b> , pp. 14723-14734 (1996)
157	Tanaka, K. et al "Effect of Cyclosporin Analogues and FK506 on Transcellular Transport of Daunorubicin and Vinblastine via P-glycoprotein" <i>Pharmaceutical Research</i> , <b>13</b> , pp. 1073-1077 (1996)
158	Rao, U. et al "Direct Demonstration of High affinity Interactions of Immunosuppressant Drugs with the Drug Binding Site of the Human P-Glycoprotein" <i>Molecular Pharmacology</i> , <b>45</b> , pp. 773-776, (1994)
159	Tinfoli, G. et al "Reversal activity of Cyclosporin A and its metabolites M1, M17 and M21 in Multidrug-resistant cells" <i>Int. J. Cancer</i> , <b>71</b> , pp. 900-906 (1997)
160	Demeule, M. et al "Molecular Interactions of Cyclosporin A with P-Glycoprotein" <i>Journal of Biological Chemistry</i> , <b>272</b> , pp. 6647-6652 (1997)
161	Saeki, T. et al "Human P-glycoprotein transports Cyclosporin A and FK506" <i>The Journal of Biological Chemistry</i> <b>268</b> pp. 6077-6080 (1993)
162	Sharon, F. et al "Synthetic hydrophobic peptides are substrates for P-Glycoprotein and stimulate drug transport" <i>Biochem. J.</i> , <b>320</b> , pp. 421-428 (1996)
163	Kiri, A. et al, "Saquinavir, an HIV Protease Inhibitor, Is Transported by P-Glycoprotein" <i>The Journal of Pharmacology and Experimental Therapeutics</i> , <b>266</b> , pp. 1439-1445 (1998)
164	Chiba, P. et al "Studies on propafenone-type modulators of multidrug resistance VI. Synthesis and pharmacological activity of compounds with varied spacer length between the central aromatic ring and the nitrogen atom" <i>Il Farmaco</i> , <b>53</b> , pp. 357-364 (1998)
165	Motonashi, N. et al "Drug Resistance Reversal, Anti-mutagenicity and Antiretroviral Effect of Phthalimido- and Chloroethyl-Phenothiazines" <i>Anticancer Research</i> , <b>17</b> , pp. 3537-3544 (1997)
166	De Jong, G. et al "Modulation of Doxorubicin Resistance in P388/ADR Cells by Ro44-5912, a Triapamil Derivative" <i>Anticancer Research</i> , <b>15</b> , pp. 911-916 (1995)
167	Camporongo, L. et al "Reversal of multidrug resistance by new dihydropyridines with low calcium antagonist activity" <i>Acta Oncologica</i> , <b>33</b> , pp. 787-791 (1994)
168	Etievant, C. et al "Requirements for P-glycoprotein recognition based on structure-activity relationships in the podophyllotoxin series" <i>Anti-Cancer Drug Design</i> , <b>10</b> , pp. 317-336 (1998)
169	Shrivastava, P. et al "Circumvention of multidrug resistance by a quinoline derivative, MS-209, in multidrug-resistant human small-cell lung cancer cells and its synergistic interaction with cyclosporin A or verapamil" <i>Cancer Chemother Pharmacol</i> , <b>42</b> , pp. 483-490 (1998)
170	Yang, J. et al "Inhibitory Effect of Alkylating Modulators on the Function of P-Glycoprotein" <i>Oncology Research</i> , <b>9</b> , pp. 477-484, (1997)
171	Thimmaiah, K. et al "Characterization of 2-Chloro-N <sup>10</sup> -Substituted Phenoxazines for Reversing Multidrug Resistance in Cancer cells" <i>Oncology Research</i> , <b>10</b> , pp. 29-41, (1998)
172	Naito, S. et al "Development of Novel Reversal Agents, Imidazothiazole Derivatives, targeting MDH1-and MRP-Mediated Multidrug Resistance," <i>Oncology Research</i> , <b>10</b> , pp. 123-132 (1998)
173	Ramu, N. et al "Circumvention of Adriamycin Resistance by Dipyridamole Analogues: a structure-activity relationship study" <i>Int. J. Cancer</i> , <b>43</b> , pp. 487-491, (1989)



OTHER DOCUMENTS *Continued*

174	Hill, B. et al "Evaluation of S9788 as a Potential Modulator of Drug Resistance against Human Tumour Sublines Expressing Differing Resistance Mechanisms <i>in vitro</i> " <i>Int. J. Cancer</i> , 55, pg. 330-337 (1993)
175	Sato, S. et al "Potentiation of vincristine and actinomycin D by a new synthetic imidazole anti-tumor agent YM534 active against human cancer cells and multidrug-resistant cells" <i>Anti-Cancer Drug Design</i> , 4, pg. 125-135, (1989)
176	Narasaki, F. et al "A novel quinoline derivative, MS-209, overcomes drug resistance of human lung cancer cells expressing the multidrug resistance-associated protein (MRP) gene" <i>Cancer Chemother Pharmacol</i> , 40, pg. 425-432 (1997)
177	Takeehita, H. et al "Avoidance of Doxorubicin Resistance in Osteosarcoma Cells Using a New Quinoline Derivative, MS-209" <i>Anticancer Research</i> , 18, pg. 739-742 (1998)
178	Boer, R. et al "Modulation in P-glycoprotein Mediated Drug Accumulation in Multidrug Resistant CCRF VCR-1000 Cells by Chemosensitizers" <i>European Journal of Cancer</i> , 32A, pg. 857-861 (1996)
179	Van Ransburg, C. et al "Novel tetramethylpiperidine-substituted phenazines are potent inhibitors of P-glycoprotein activity in a multidrug resistant cancer cell line" <i>Anticancer Drugs</i> , 8, pg. 708-713 (1997)
180	Choi, S. et al "The bisbenzylisoquinoline alkaloids, tetrastine and fargylinoline, enhance the cytotoxicity of multidrug resistance-related drugs via modulation of P-glycoprotein." <i>Anticancer Drugs</i> , 9, pg. 255-261 (1998)
181	Abdorrabi, M. et al "Comparative <i>in vitro</i> evaluation of dithiane analogs of tiapamil, Ro 11-2933, Ro 44-5911 and Ro 44-5912 as multidrug resistance modulators" <i>Anti-Cancer Drugs</i> , 7, pg. 430-436 (1996)
182	Kim, S. et al "Circumvention of drug resistance in cancer cells by a new fluoropyrimidine analogue" <i>Experimental and molecular Medicine</i> , 28, pg. 119-123, (1996)
183	Christensen, J. et al "Reversal of multidrug resistance by derivatives of acrivastine: a study of structure-activity relationships of P glycoprotein inhibitors <i>in vitro</i> and <i>in vivo</i> " <i>Oncology Reports</i> , 4, pg. 1353-1360 (1997)
184	Thimmaiah, K. et al "Structural Determinants of Phenoxazine Type Compounds Required to Modulate the Accumulation of Vinblastine and Vincristine in Multidrug resistant cell lines" <i>Cancer Communications</i> , 2, pg. 249-259, (1990)
185	Smith, A. et al "Availability of PSC033, a Substrate and Inhibitor of P-Glycoproteins, in Various Concentrations of Serum" <i>Journal of the National Cancer Institute</i> , 90, pg. 1161-1166, (1998)
186	Sepioldi, J. et al "Peptide derivatives Against Multidrug Resistance" <i>Peptides, Proceedings of the 24<sup>th</sup> European Peptide Symposium</i> , pg. 801-802, (1998)
187	Suzuki, T. et al "Structure-Activity Relationship of Newly Synthesized Quinoline derivatives for Reversal of Multidrug Resistance in Cancer" <i>J. Med. Chem.</i> , 40, pg. 2047-2052 (1997)
188	Chibo, P. et al "Substituted 4-Acylpyrazoles and 4-Acylpyrazolones" Synthesis and Multidrug Resistance-Modulating Activity" <i>J. Med. Chem.</i> , 41, pg. 4001-4011 (1998)
189	Suzuki, T. et al "Synthesis of Glucuronides of multidrug resistance Reversing Drug MS-209" <i>Bioorganic &amp; Medicinal Chemistry Letters</i> , 2, pg. 659-662 (1999)
190	Nakamura, S. et al "Effects of Isoquinolinesulphonamide Compounds on Multidrug-resistant P388 cells" <i>J. Pharm. Pharmacol</i> , 45, pg. 268-273 (1993)
190	Ogino, J. et al "Dendroamides, New Cyclic Hexapeptides from a Blue-Green Alga. Multidrug-Resistance Reversing activity of dendroamide A." <i>J. Nat. Prod.</i> , 59, pg. 581-586 (1996)
191	Kim, E. et al. "A New Sesquiterpene Ester from <i>Celastrus orbiculatus</i> Reversing Multidrug Resistance in cancer Cells" <i>J. Nat. Prod.</i> , 61, pg. 108-111 (1998)
192	Lehner, M. et al "Phase II trial of dexverapamil and epirubicin in patients with non-responsive metastatic breast cancer" <i>British Journal of Cancer</i> , 77, pg. 1155-1163 (1998)
193	Dale, I. et al "Reversal of P-glycoprotein-mediated multidrug resistance by XR9051, a novel diketopiperazine derivative" <i>British Journal of Cancer</i> , 78, pg. 885-892 (1998)
194	Budworth, J. et al "Comparison of Staurosporine and four analogues: their effects on growth, modamine 123 retention and binding to P-glycoprotein in multidrug resistant MCF-7/Adr cells" <i>British Journal of Cancer</i> , 73, pg. 1063-1068 (1996)
195	Hirwitz, L. et al "Can prenylcystines be exploited as ligands for mammalian multidrug-resistance transporters?" <i>Chemistry &amp; Biology</i> , 4, pg. 711-715 (1997)
196	Gekeler, V. et al "Effects of the selective bisindolylmaleimide protein kinase C inhibitor GF109203X on P-glycoprotein-mediated multidrug resistance" <i>British Journal of Cancer</i> , 74, pg. 897-905 (1996)
197	Newman, R. et al "MDL 201307: a novel benzothiazepine modulator of multiple drug resistance" <i>Journal of Experimental Therapeutics &amp; Oncology</i> , 7, pg. 109-116 (1996)
198	Jachez, B. et al "SDZ 260-125: a cyclopeptide endowed with an <i>in vitro</i> cyclosporin A-like profile of activity for the reversion of the P-glycoprotein-mediated multidrug resistance of tumor cells" <i>Anti-cancer drugs</i> , 5, pg. 313-320 (1994)
199	Jachez, B. et al "Reversion of the P-glycoprotein-mediated multidrug resistance of cancer cells by FK-506 derivatives" <i>Anti-cancer Drugs</i> , 4, pg. 223-229 (1993)
200	Fan, D. et al "Reversal of multidrug resistance in murine fibrosarcoma cells by thioxanthene flupentixol" <i>Investigational New Drugs</i> , 12, pg. 185-195, (1994)

OTHER DOCUMENTS *Continued*

201	Molnar, J. et al "Inhibition of the Transport Function of Membrane Proteins by Some Substituted Phenothiazines in <i>E. Coli</i> and Multidrug Resistant Tumor Cells" <b>Anticancer Research</b> , 17, pg. 481-486 (1997)
202	Teodori, E. et al "Design, Synthesis, and in Vitro Activity of Catamphiphilic reverts of Multidrug Resistance: Discovery of a Selective, Highly Efficacious Chemosensitizer with Potency in the Nanomolar Range" <b>J. Med. Chem.</b> , 42, pg. 1687-1697, (1999)
203	Van Asperen, J. et al "The Pharmacological Role of P-Glycoprotein in the Intestinal Epithelium". <b>The Italian Pharmacological Society</b> , (1998)
204	Wacher, V. et al "Role of P-Glycoprotein and Cytochrome P450 3A in Limiting Oral Absorption of Peptides and Peptidomimetics" <b>Journal of Pharmaceutical Sciences</b> 97, pg. 1322-1330, (1999)
205	Matsuzaki, J. et al "Contribution of P-glycoprotein to Bunitrolol Efflux across Blood-Brain Barrier" <b>Biopharmaceutics and Drug Disposition</b> , 20, pg. 85-90(1999)
206	Sanglard, D. et al "Mechanisms of Resistance to azole Antifungal Agents in <i>Candida albicans</i> Isolates from AIDS Patients Involve Specific Multidrug Transporters" <b>Antimicrobial Agents and Chemotherapy</b> , 39, pg. 2378-2386 (1995)
207	Li, X. et al "Role of Efflux Pump(s) in Intrinsic Resistance of <i>Pseudomonas aeruginosa</i> : Active Efflux as a contributing Factor a B-Lactam Resistance" <b>Antimicrobial Agents and Chemotherapy</b> , 38, pg. 1742-1752 (1994)
208	Van Veen, H. et al "The ABC family of multidrug transporters in microorganisms" <b>Biochimica et Biophysica Acta</b> , 1365, pg. 31-36 (1998)
209	Kim, A. et al "Saquinavir, an HIV Protease Inhibitor, is Transported by P-Glycoprotein". <b>Journal Pharm. And Experimental Therapeutics</b> , 286, pg. 1439-1445 (1998)
210	Lee, I. et al "Protease Inhibitors and the MDR1 Multidrug Transporter" <b>The Journal of Clinical Investigation</b> , 107, pg. 287-288 (1998)
211	Renau, T. et al "Chapter 12. Antimicrobial Potentiation Approaches: Targets and Inhibitors" <b>annual Reports in Medicinal Chemistry</b> , 33, pg. 121-129 (1998)
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